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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/761,370
Filing Date: January 22, 2004
Appellant(s): WALLACH ET AL.

Roger L. Browdy
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 07/21/2009 appealing from the Office action mailed on 04/29/2008.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Yongan, L. "Identification and characterization of cellular proteins which interact with adenovirus E3 14.7 KDA protein an antagonist of TNF-alpha" PhD thesis, published in OCLC's Experimental Thesis Catalog and also issued on microfilm in 1966; Abstract).

Yongan, L. et al. "Interaction of the adenovirus E3 14.7-kilodalton protein with a novel tumor necrosis factor alpha-inducible cellular protein containing leucine zipper domains" Mol Cell Biol, March 1st, 1998, vol. 18, pp. 1601-1610.

Ellis, J.H. et al. ("Engineered anti-CD38 monoclonal antibody for immunotherapy of multiple myeloma" J Immunol, 1995, vol. 155, pp. 925-937.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 17-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yongan (PhD thesis, published in OCLC's Experimental Thesis Catalog and also issued on microfilm in 1966; Abstract), in view of both Yongan et al. (Mol Cell Biol, March 1st, 1998, 18: 1601-1610) and Ellis et al. (J Immunol, 1995, 155: 925-937).

Yongan et al. teach that the data from their paper is identical to the data from the PhD thesis submitted by Yongan in 1996 (see Yongan et al., p. 1602, column 1, third full paragraph). Therefore, via Yongan et al., Yongan's 1996 PhD thesis, teaches identification of Fip-2, a novel protein containing multiple leucine zipper domains, which is one of the cellular targets of the adenoviral protein Ad E3-14.7K, an inhibitor of TNF-α-induced apoptosis (Abstract, p. 1602, column 1, p. 1606, column 2). Yongan teaches that the C-terminus of Fip-2 is necessary for its interaction with Ad E3-14.7K (p. 1606, column 2, last paragraph. p. 1607, columns 1 and 2). Yongan teaches that Fip-2 has leucine zipper domains, which could be implicated in signaling (p. 1608, column 2, second full paragraph).

Yongan does not teach anti-Fip-2 antibodies. However, Yongan teaches expressing Fip-2 as a recombinant protein comprising a T7 tag and using anti-T7 tag antibodies to study recombinant Fip-2 in cells expressing the recombinant Fip-2 (p. 1603, column 2, last paragraph, p. 1606, Fig. 3). By reading Yongan, one of skill in the art would have known that antibodies against Fip-2 could be used to study interaction between intracellular proteins involved in signaling and their co-localization inside the cell (p. 1603, column 2, p. 1606, column 1). It would have been obvious to one of skill

in the art, at the time the invention was made, to raise polyclonal antibodies directed to Fip-2, with a reasonable expectation of success. One of skill in the art would have been motivated to do so in order to study the localization of native Fip-2 and its interaction with the cellular proteins involved in TNF-α signaling pathway. With respect to the limitations of monoclonal and chimeric antibodies (claims 17 and 18) and of a detectable label (claim 19) obtaining such was routine in the prior art (see for example Ellis et al., Abstract, p. 926, columns 1 and 2). It is noted that, since Yongan teaches the importance of the leucine zipper and C-terminal domains, one of skill in the art would have been motivated to obtain monoclonal antibodies against these domains to study their role in Fip-2 function. Furthermore, one of skill in the art would have been motivated to use a chimeric antibody in order to obtain a humanized antibody that could be used for therapy in humans. One of skill in the art would have been motivated to use a label in order to localize the protein inside the cell. It is noted that all these techniques are routine in the art, and therefore, one of skill in the art would have been expected to have a reasonable expectation of success in obtaining these antibodies.

It is noted that the specification teaches that the leucine zipper domain of Fip-2 is preserved in RAP-2 (encoded by SEQ ID NO: 4), wherein the leucine zipper domain is located in the C-terminal domain of RAP-2; the specification also teaches that the C-terminal amino acids are identical in Fip-2 and Rap-2 (see paragraphs 0019 and 0088; Fig. 3B). Therefore, anti-Fip-2 polyclonal antibodies (which necessarily comprise antibodies against the leucine zipper and the C-terminal domains) and monoclonal

antibodies directed against the leucine zipper and C-terminal domains of Fip-2 must necessarily be specific for RAP-2 (claim 1).

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

(10) Response to Argument

Appellant's arguments

Appellant argues that the subgenus of antibodies within the scope of 1laim 1 would not have been obvious from the genus of antibodies allegedly made obvious by the combined teachings of the prior art.

Applicant points out that it is essentially the Examiner's position that it would have been obvious to raise antibodies against Fip-2 and that among these antibodies are antibodies that will also bind RAP-2, which would thus fall within the scope of claim 1. Thus, the Examiner concludes that the subject matter of claim 1 is *prima facie* obvious and unpatentable under 35 USC 103. While Applicant will argue below that the Examiner has not established a *prima facie* case that antibodies can be raised against Fip-2 that will also bind RAP-2, for the purpose of the present argument, Applicant will concede that the Examiner has established this. However, even if such antibodies exist, the subgenus (or subset) of the antibodies encompassed by claim 1 possess a property that would have been totally unexpected from the genus (or set) of antibodies allegedly made obvious by the combined teachings of the prior art. Hence, the claimed antibodies are unobvious. That a genus may be obvious does not necessarily make

obvious every species within that genus. At best, the Examiner alleges that the genus of anti-Fip-2 antibodies is made obvious by the combined teachings of the prior art. However, the present claims are not directed to such a genus and would not be anticipated if such a genus were part of the prior art. The present claims are effectively species or subgenus claims directed to that relatively small subset (if it exists at all) of the prior art genus of anti-Fip-2 antibodies that will also bind to RAP-2. The antibodies that are allegedly prima facie obvious from the combined teachings of the prior art would all bind to Fip-2. Because Fip-2 has large areas that are not homologous to RAP-2 (see the sequence alignment of Figure 3(B), discussed below), it would not be expected that every antibody raised against Fip-2 will necessarily bind RAP-2. Thus, most of the antibodies allegedly made prima facie obvious by the combined teachings of the prior art will not fall within the scope of any of the present claims. This is why the antibodies allegedly made *prima facie* obvious by the combined teachings of the prior art represent a genus of anti- Fip-2 antibodies that include a majority of antibodies that do not bind RAP-2. To the extent that there are any anti-RAP-2 antibodies within this genus, they represent only a species or subgenus thereof. This subgenus is not per se obvious from the existence of or obviousness of an genus of antibodies that encompasses them. Attention is directed to the guidelines of the MPEP at §2144.08 directed to obviousness of species when the prior teaches a genus. Note particularly Section II where it states:

> The patentability of a claim to a specific compound or subgenus embraced by a prior art genus should be analyzed no differently than any other claim for purposes of 35 U.S.C. 103. "The section 103 requirement of unobviousness is no different in chemical cases than with respect to other categories of patentable inventions." In re Papesch, 315 F.2d 381, 385, 137 USPQ 43, 47 (CCPA 1963). A determination of patentability under 35

> U.S.C. 103 should be made upon the facts of the particular case in view of the totality of the circumstances. See, e.g., In re Dillon, 919 F.2d 688, 692-93, 16 USPQ2d 1897, 1901 (Fed. Cir. 1990) (in banc). Use of per se rules by Office personnel is improper for determining whether claimed subject matter would have been obvious under 35 U.S.C. 103. See, e.g., In re Brouwer, 77 F.3d 422, 425, 37 USPQ2d 1663, 1666 (Fed. Cir. 1996); In re Ochiai, 71 F.3d 1565, 1572, 37 USPQ2d 1127, 1133 (Fed. Cir. 1995); In re Baird, 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994). The fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient by itself to establish a prima facie case of obviousness. In re Baird, 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994) ("The fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious."); In re Jones, 958 F.2d 347, 350, 21 USPQ2d 1941, 1943 (Fed. Cir. 1992) (Federal Circuit has "decline[d] to extract from Merck [& Co. v. Biocraft Laboratories Inc., 874 F.2d 804, i0 USPQ2d 1843 (Fed. Cir. 1989)] the rule that... regardless of how broad, a disclosure of a chemical genus renders obvious any species that happens to fall within it."). See also In re Deuel, 51 F.3d 1552, 1559, 34 USPQ2d 1210, 1215 (Fed. Cir. 1995).

Accordingly, even if it is determined that the Examiner has established a *prima facie* case that the entire genus of anti- Fip-2 antibodies would have been obvious, that does not establish a prima facie case of obviousness for every species or subgenus within that genus. See In re Baird, supra. The present claims are not directed to the genus of anti-Fip-2 antibodies. The present claims are specifically directed to the subgenus of those anti-Fip-2 antibodies that binds RAP-2.

The Examiner has provided no rationale whatsoever why the claimed subgenus of RAP-2 binding antibodies would have been obvious from the genus of anti-Fip-2 antibodies. The Examiner seems to assume that there is some kind of a per se rule that if she establishes the obviousness of a genus, every species or subgenus thereof is necessarily obvious. But the above-quoted section §2144.08 of the MPEP and the cases cited therein establish that there is no such per se rule. For this reason alone, the Examiner has not met her burden of establishing a *prima facie* case of obviousness for

the presently claimed subgenus of the genus of antibodies allegedly made obvious by the combined teachings of the prior art.

Furthermore, the claimed subject matter could not possibly have been obvious from the genus in view of the fact that the subgenus has properties which are unexpected from any consideration of the properties of the genus. The properties of the claimed subgenus necessarily include, by definition, the property of binding RAP-2. The fact that there may exist a subgenus of antibodies, within the genus of anti-Fip-2 antibodies, that also bind RAP-2, was unknown at the time of the present invention. Even if the Examiner had submitted a rationale to establish a *prima facie* case of obviousness for the presently claimed subgenus of the antibodies of the prior art, such a *prima facie* case of obviousness can be rebutted by a showing of unexpected results. Note MPEP 2145 where it states:

> Rebuttal evidence may also include evidence that the claimed invention yields unexpectedly improved properties or properties not present in the prior art. Rebuttal evidence may consist of a showing that the claimed compound possesses unexpected properties. [In re] Dillon, [919 F.2d 688, 692-3, 16 USPQ2d 1897, 1901 (Fed. Cir. 1990)].

By definition, all of the antibodies within the scope of claim 1 bind RAP-2. If any of the antibodies allegedly made prima facie obvious by the combined teachings of the prior art have the property of binding RAP-2, this would have been an unexpected property at the time of the present invention as the existence of RAP-2 was not known to the prior art at the time of the present invention. While it would have been expected that any antibody raised against Fip-2 would bind to Fip-2, those antibodies which also bind to RAP-2 possess the unexpected property of being able to bind to RAP-2. It is only by hindsight that the Examiner reaches the conclusion that some of the antibodies

that can be raised against Fip-2 may bind to RAP-2; but if they do, this is necessarily unexpected as RAP-2 did not exist in the prior art. The fact that some of the antibodies that can be raised against Fip-2 can be used to fish RAP-2 out of a mixture of proteins, could not possibly have been expected at the time of the present invention as the existence of RAP-2 was not known. Thus, the subset of anti-Fip-2 antibodies that also bind to RAP-2 (assuming that such a subset even exists) would not have been obvious since one of ordinary skill in the art would have no way to identify any antibody that falls within this subset that binds to RAP-2, as RAP-2 is not part of the prior art.

In the Advisory Action, the Examiner states that the present claims do not recite that the antibody recognizes RAP- 2 without recognizing Fip-2. This is correct and there is a good reason for this: it does not matter whether any of the antibodies of the present invention recognize Fip-2. The present claims do not intend to exclude antibodies that recognize Fip-2. It is only necessary that the present claims cover antibodies that recognize RAP-2. If any of such antibodies also recognize Fip-2, this is irrelevant to the scope of claim 1. Moreover, that fact does not affect the patentability of those antibodies for the reasons discussed above. As discussed above, the prior art does not make obvious any of the specific antibodies allegedly made obvious by the combined teachings of the prior art which happen to recognize RAP-2. Those are the only antibodies covered by the present claims.

Accordingly, considering all of the evidence of record, a person of ordinary skill in the art would not have considered a claim to the subgenus of anti-RAP-2 antibodies to have been obvious from any reading of Yongan 1996, Yongan 1998 and Ellis.

Appellant argues that it is not prima facie obvious that any antibody that can be raised against Fip-2 will necessarily bind to Rap-2. The Examiner has stated in the Official Action of July 26, 2007:

> It is noted that the specification teaches that the leucine zipper domains and the C-terminus of Rap-2 (encoded by SEQ ID NO. 4) and Fip-2 are conserved (p. 14, paragraph 0019 and p. 15, paragraph 0021) and therefore anti-Fip-2 antibodies recognizing these domains would necessarily be specific for Rap-2 (claim 1).

Paragraph [0019] referred to by the Examiner states that the global alignment of the amino acid sequences of RAP-2 and Fip- 2 are shown in Figure 3. Paragraph [0088] clarifies that the alignment of the sequence of Fip-2 and the sequence of RAP-2 (SEQ ID NO: 4) appears in Figure 3B. Thus, it is not necessary to rely on the characterizations in paragraphs [0019] and [0021], as done by the Examiner, as one can actually see what is identical and what is preserved in Figure 3B. It can be seen from a review of Figure 3B that the only area of sequence identity of greater than 5 amino acids between RAP-2 and Fip-2 is the 8 amino acid region from amino acid 408 to 415 of RAP-2 and amino acid 566 to 573 of Fip-2.

The Examiner is essentially taking the position that at least one antibody that can be raised against Fip-2 would inherently bind to RAP-2. However, the Examiner has not satisfied her burden of establishing that such inherency is necessarily the case. Thus, even if this were an anticipation reference and one of the primary references disclosed making antibodies against Fip-2, such a rejection based on inherency must fall as the Examiner cannot establish that such inherency is inevitable and certain. Note In re Oelrich, 212 USPQ 323, 326 (CCPA 1981), where it states:

> Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.

It is possible that amino acids 566-573 of Fip-2 are immunogenic and will cause an antibody to be raised against them. However, it is also possible that this sequence is not exposed on the surface of the Fip-2 protein and therefore would not generate an antibody specific thereto when using Fip-2 as an immunogen. Furthermore, even if it were possible to raise an antibody that recognizes amino acids 566-573 of Fip-2, it is possible that such an antibody would not bind to the same sequence that is part of RAP-2. It is also possible that, although the amino acids are the same, the amino acids are on the surface of Fip-2 but not necessarily on the surface of RAP-2, in which case the antibody raised against Fip-2 would not recognize the same sequence that is hidden in RAP-2. It is not sufficient that a certain thing may result from a given set of circumstances to establish inherency, it must be inevitable. See also MPEP §2112 IV which states:

> Also, "[a]n invitation to investigate is not an inherent disclosure" where a prior art reference "discloses no more than a broad genus of potential applications of its discoveries." Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings, 370 F.3d 1354, 1367, 71 USPQ2d 1081, 1091 (Fed. Cir. 2004) (explaining that "[a] prior art reference that discloses a genus still does not inherently disclose all species within that broad category" but must be examined to see if a disclosure of the claimed species has been made or whether the prior art reference merely invites further experimentation to find the species.

Here, the Examiner is presenting nothing more than an invitation to investigate whether it is possible to raise an antibody against Fip-2 that would bind to RAP-2. In view of the only sporadic homology between RAP-2 and Fip-2, as can be clearly seen in Figure 3(B) of the present specification, the Examiner has not established that there is

certainty that any antibody raised against Fip-2 would necessarily bind to RAP-2. Accordingly, the Examiner has not satisfied her burden of establishing a *prima facie* case that the combined teachings of the prior art would necessarily include any antibodies that would bind to RAP-2. One of ordinary skill in the art would not consider that antibodies raised against Fip- 2 as an immunogen would necessarily produce anti-Fip-2 antibodies that would necessarily recognize a domain which also appears on RAP-2 or that such antibodies, even if they were raised, would necessarily be specific for RAP-2.

Appellant argues that claims 17 and 18 are patentable in their own right as monoclonal antibodies, or fragments thereof, would not have been obvious from the combined teachings of the prior art. Appellant argues that one of skill in the art would understand that in any given round of hybridoma production, there is no guarantee that any of the monoclonal antibodies that are obtained by screening against Fip-2 would necessarily be directed to that portion of Fip-2 that happens to overlap with RAP-2 (assuming that any such antibodies even exist). It is not inherent that any such monoclonal antibodies would be obtained. Certainly, one of skill in the art would understand that it is common practice in the antibody art that antibodies not found in one round of hybridomas may be found in another. In any event, one of skill in the art would never know whether any given hybridoma found by the combination of references suggested by the Examiner would fall within the scope of the present claims. This does not even establish a *prima facie* case of obviousness.

The Examiner has not discussed whether the regions of overlap are particularly immunogenic. One cannot simply assume that monoclonal antibodies can be raised against every possible region of a protein. Some regions may be folded within the protein or be obscured. Thus, there is no certainty that a monoclonal antibody to the overlapping region would even be raised when looking generally for monoclonal antibodies that bind to Fip-2, let alone whether it would be obvious to select for that monoclonal antibody that happens to be directed to such an overlapping region.
A monoclonal antibody, by definition, is the subject of selection. Many antibodies may be raised against Fip-2. A monoclonal antibody is a clone of only a single antibody that has been raised against Fip-2, which has been selected for its ability to bind to Fip-2. Thus, by definition, some degree of selection is required in order to obtain a monoclonal antibody that binds to Fip-2. The present claims require that the monoclonal antibody bind RAP-2. Thus, the monoclonal antibody of the combined teachings of the prior art, selected for its capability of binding to FIP-2, must also be subject to selection for binding to RAP-2. It would not be obvious to perform this additional degree of selection to identify those specific antibodies from among those that are capable of binding to Fip-2 that may also bind to RAP-2. Accordingly, monoclonal antibodies are one step further away from the combined teachings of the prior art than the general antibodies of claim 1. For this reason, claim 17 is unobvious from the combined teachings of the prior art in its own right as well as for the reasons discussed hereinabove for claim 1 from which it depends.

The same is true for the chimeric antibodies of claim 18. To obtain a chimeric antibody, one must start with a monoclonal antibody. Thus, the chimeric antibodies of claim 18 are independently patentable for the same reasons as discussed above for claim 17.

Response to Appellant's arguments

Appellant argues that the subgenus of antibodies recited in the claims are not obvious because Fip-2 has large areas which are not homologous to RAP-2, and therefore, most of the antibodies taught by the combination of the cited references would not fall within the scope of the present claims. In response to this argument it is noted that claim 1 broadly encompasses any antibody type, including polyclonal antibodies. A polyclonal anti-Fip-2 antibody preparation is a mixture of antibodies; because of sequence homology between the C-terminal of FIP-2 and RAP-2, this polyclonal antibody preparation necessarily comprises antibodies which also recognize RAP-2 (i.e., the genus necessarily comprises the subgenus). The argument that the subgenus does not represent the majority of the genus is irrelevant because the claims do not require that the antibodies specific for RAP-2 (i.e., the subgenus) be isolated from the polyclonal preparation (i.e., the genus). With respect to Appellant's citation from MPEP 2144.08, such is applicable when the prior art does not specifically discloses the claimed species. In the instant case, since the genus necessarily comprises the subgenus, there is no need to specifically select the subgenus. By obtaining the polyclonal antibody, one of skill in the art would also obtain an antibody

specific for RAP-2. Therefore, the subgenus of antibodies encompassed by claim 1 is not totally unexpected from the genus. The claimed invention is rendered *prima facie* obvious.

Appellant argues that, since RAP-2 was unknown at the time the invention was made, the property of binding RAP-2 would have been unexpected, i.e., it would have been unexpected that that any antibody directed against Fip-2 would also bind RAP-2. In response to this argument it is noted that unexpected results relate to "unexpectedly improved properties or properties not present in the prior art" (see paragraph from MPEP 2145 cited by Appellant). In the instant case, there is no showing of any improved property (it is noted that the specification only provides hypothetical examples of obtaining polyclonal and monoclonal antibodies; the specification does not provide any example of polyclonal or monoclonal antibody directed to RAP-2 which would exhibit unexpectedly improved properties). Furthermore, the property of binding RAP-2 is inherent to the polyclonal anti-Fip-2 antibody preparation taught by the prior art, i.e., the property is present in the prior art.

Appellant argues that the fact that anti-FIP2 antibodies could be used to isolate Rap-2 from a mixture of proteins could not have been expected at the time the invention was made because RAP-2 was not known. This argument is irrelevant because the instant invention is not drawn to a method of isolating RAP-2; the instant rejection does not propose such. Similar considerations apply to Appellant's arguments that it would not have been obvious to one of skill in the art to identify any antibody capable of binding RAP-2. The rejection does not state that the antibody must be identified by its

ability to bind RAP-2. The rejection states that anti-RAP-2 antibodies are inherently present in a polyclonal antibody preparation.

Appellant argues that the Examiner used hindsight in making the instant rejection. In response to this, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Appellant argues that the only area of sequence identity of greater than 5 amino acids between RAP-2 and Fip-2 is the 8 amino acid region from amino acid 408 to 415 of Rap-2 and amino acid 566 to 573 of Fip-2. While this is true, it is noted that the C-terminal domains of RAP-2 and Fip-2 are approximately 57% homologous and comprise several identical stretches of 4-5 amino acids in length, which constitute epitopes for eliciting immune responses (see Fig. 3B).

Appellant argues that the Examiner cannot establish that inherency is inevitable and certain. Specifically, Appellant argues that, although amino acids 566-573 of Fip-2 could be immunogenic, it is possible that this sequence could not generate antibodies because it is not exposed on the surface. Appellant also argues that it would be possible to obtain an antibody directed to the amino acids 566-573 of Fip-2, this antibody might not bind RAP-2 because the RAP-2 amino acid sequence corresponding to the amino acids 566-573 of Fip-2 might be hidden in RAP-2. These arguments are

not found persuasive because they are just arguments not supported by any evidence. Even assuming for the sake of the argument that this would be true, as noted above, the C-terminal domain of Fip-2 shares many epitopes with the C-terminal domain of RAP-2; for certain, at least one of these epitopes would be able to elicit an antibody response.

With respect to the monoclonal antibody, Appellant argues that it would not be inherent that such an antibody could be obtained. This is just an argument not supported by any evidence. Yongan clearly teaches the importance of the C-terminal domain of Fip-2; therefore, one of skill in the art would have been motivated to obtain monoclonal antibodies directed against this domain (see the rejection above). Obtaining monoclonal antibodies directed to specific sequences in proteins was routine in the prior art.

Appellant argues that there is no certainty that a monoclonal antibody directed to the homologous sequences because some of them might be folded within the protein. This is again just an argument not supported by any evidence. Even assuming that some of these sequences would not be accessible, one would have expected to be reasonably successful in obtaining monoclonal antibodies directed against the remaining exposed epitopes. Alternately, it would have been within the knowledge and capabilities of one of skill in the art to raise antibodies against desired peptides (i.e., exposed epitopes) as doing such was routine in the prior art.

Applicant argues that, since the instant claims require that the monoclonal antibody binds RAP-2, the monoclonal antibody taught by the combined teachings of

the prior art must also be subjected to selection for binding to RAP-2. This argument is not found persuasive. The claims do not require selection by binding to RAP-2. One of skill in the art would have been motivated to raise various antibodies against the C-terminal domain of Fip-2 because the C-terminal domain of Fip-2 is important for its function (see the rejection above). A second selection step by binding to RAP-2 is not necessary because a monoclonal antibody directed against the common epitopes would necessarily bind RAP-2.

For these reasons, the claimed antibodies are rendered obvious by the cited documents.

In conclusion, the Office has properly applied the test for obviousness set forth in *Graham v. John Deere Company* and established a *prima facie* case of obviousness over the claims on appeal based on the teachings of Yongan (PhD thesis, published in OCLC's Experimental Thesis Catalog and also issued on microfilm in 1966; Abstract), in view of both Yongan et al. (Mol Cell Biol, March 1st, 1998, 18: 1601-1610) and Ellis et al. (J Immunol, 1995, 155: 925-937).

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Ileana Popa/

Primary Examiner, Art Unit 1633

Conferees:

/Joseph T. Woitach/

Supervisory Patent Examiner, Art Unit 1633

/Ram R. Shukla/

Supervisory Patent Examiner, Art Unit 1644